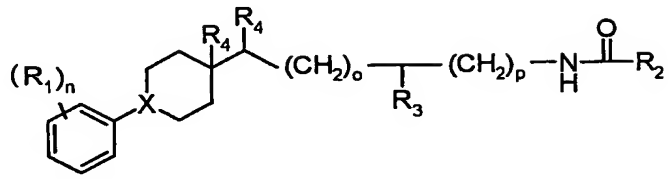
Claims

1. A compound of structural formula (I):



(I)

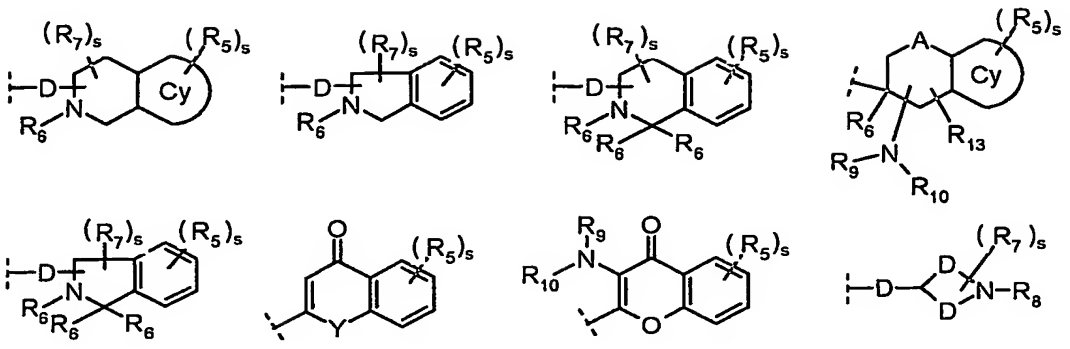
or a pharmaceutically acceptable salt or a solvate thereof, wherein

R_1 is independently:

hydrogen,
hydroxy,
cyano,
nitro,
halo,
alkyl,
alkoxy,
haloalkyl,
(D)-$C(O)R_{15}$,
(D)-$C(O)OR_{15}$,
(D)-$C(O)SR_{15}$,
(D)-C(O)-heteroaryl,
(D)-C(O)-heterocyclyl,
(D)-$C(O)N(R_{15})_2$,
(D)-$N(R_{15})_2$,
(D)-$NR_{15}COR_{15}$,

(D)-$NR_{15}CON(R_{15})_2$,
(D)-$NR_{15}C(O)OR_{15}$,
(D)-$NR_{15}C(R_{15})=N(R_{15})$,
(D)-$NR_{15}C(=NR_{15})N(R_{15})_2$,
(D)-$NR_{15}SO_2R_{15}$,
(D)-$NR_{15}SO_2N(R_{15})_2$,
(D)-NR_{15}(D)-heterocyclyl,
(D)-NR_{15}(D)-heteroaryl,
(D)-OR_{15},
OSO_2R_{15},
(D)-$[O]_v$(C_3 - C_7 cycloalkyl),
(D)-$[O]_v$(D)aryl,
(D)-$[O]_v$(D)-heteroaryl,
(D)-$[O]_v$(D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen when v=1),
(D)-SR_{15},
(D)-SOR_{15},
(D)-SO_2R_{15} or
(D)-$SO_2N(R_{15})_2$,
wherein alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl and heteroaryl are unsubstituted or substituted;

R_2 is:



R_3 is independently:

(D)-aryl or

(D)-heteroaryl,

wherein aryl and heteroaryl are unsubstituted or substituted;

R_4 is H or a bond;

each R_5 is independently:

hydrogen,

halo,

alkyl,

haloalkyl,

hydroxy,

alkoxy,

S-alkyl,

SO_2-alkyl,

O-alkenyl

S-alkenyl

$NR_{15}C(O)R_{15}$,

$NR_{15}SO_2R_{15}$,

$N(R_{15})_2$,
(D)-cycloalkyl or
(D)-aryl (wherein aryl is phenyl or naphthyl),
(D)-heteroaryl or
(D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen), and
wherein aryl, heteroaryl, heterocyclyl, alkyl or cycloalkyl is unsubstituted or substituted, and two adjacent R_5 may form a 4- to 7-membered ring;

each R_6 is independently:
hydrogen,
alkyl,
C(O)-alkyl,
(D)-aryl or
cycloalkyl;

each R_7 is independently:
hydrogen,
alkyl,
(D)-aryl,
(D)-heteroaryl,
(D)-$N(R_9)_2$,
(D)-$NR_9C(O)$ alkyl,
(D)-NR_9SO_2 alkyl,
(D)-$SO_2N(R_9)_2$,
(D)-$(O)_r$ alkyl,
(D)-$(O)_r$(D)-NR_9COR_9,
(D)-$(O)_r$(D)-$NR_9SO_2R_9$,
(D)-$(O)_r$-heterocyclyl or
(D)-$(O)_r$(alkyl)-heterocyclyl;

each R_8 is independently:

hydrogen,
alkyl,
(D)-aryl,
C(O) alkyl,
C(O)-aryl,
SO_2-alkyl or
SO_2-aryl;

R_9 and R_{10} are each independently:

hydrogen,
alkyl or
cycloalkyl, or
R_9 and R_{10} together with the nitrogen to which they are attached form a 5- to 8-membered ring optionally containing an additional heteroatom selected from O, S and NR_6,
wherein alkyl and cycloalkyl are unsubstituted or substituted;

R_{13} is:

hydrogen or
alkyl;

each R_{15} is independently:

hydrogen,
alkyl,
haloalkyl,
(D)-cycloalkyl,
(D)-aryl (wherein aryl is phenyl or naphthyl),
(D)-heteroaryl or

(D)-heterocyclyl,

wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen, and wherein aryl, heteroaryl, heterocyclyl, alkyl and cycloalkyl is unsubstituted or substituted;

Cy is:

aryl,

5- or 6-membered heteroaryl,

5- or 6-membered heterocyclyl or

5- or 7-membered carbocyclyl;

A is a bond, O, $S(O)_u$, NR_8 or CH_2;

D is a bond or alkylene;

X is N or CH;

Y is O or NR_9;

n is 1 - 4;

o is 0 - 2;

p is 0 - 2;

r is 0 or 1;

s is 0 - 5;

u is 0 - 2;

v is 0 or 1.

2. The compound of claim 1, wherein

each R_1 is independently:

hydrogen,

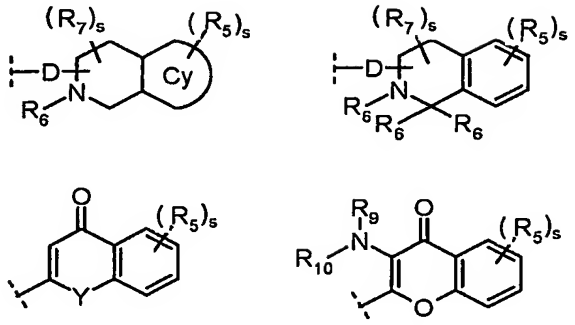
hydroxy,

cyano,

nitro,

halo,
alkyl,
alkoxy,
haloalkyl,
(D)-$N(R_{15})_2$,
(D)-$NR_{15}COR_{15}$,
(D)-$NR_{15}CON(R_{15})_2$,
(D)-$NR_{15}C(O)OR_{15}$,
(D)-$NR_{15}C(R_{15})=N(R_{15})$,
(D)-$NR_{15}C(=NR_{15})N(R_{15})_2$,
(D)-$NR_{15}SO_2R_{15}$,
(D)-$NR_{15}SO_2N(R_{15})_2$ or
(D)-heterocyclyl;

R_2 is:



R_3 is (CH_2)-phenyl or (CH_2)-naphthyl, unsubstituted or substituted with one to three substituents selected from the group consisting of cyano, nitro, perfluoroalkoxy, halo, alkyl, (D)-cycloalkyl, alkoxy and haloalkyl;

each R_5 is independently:
hydrogen,

halo,
alkyl,
haloalkyl,
hydroxy,
alkoxy,
S-alkyl,
SO_2-alkyl,
O-alkenyl or
S-alkenyl;

each R_6 is independently:
hydrogen or
alkyl;

each R_7 is independently:
alkyl,
hydrogen,
(D)-aryl,
(D)-heteroaryl,
(D)-$N(R_9)_2$,
(D)-$NR_9C(O)$alkyl or
(D)-NR_9SO_2alkyl;

R_9 and R_{10} are each independently:
hydrogen,
alkyl or
cycloalkyl, or
R_9 and R_{10} together with the nitrogen to which they are attached form a 5- to 7-membered ring optionally containing an additional heteroatom selected from O, S and NR_6;

each R_{11} is independently:
alkyl,
OR_{12},
(D)-aryl,
(D)-cycloalkyl,
(D)-heteroaryl or
halo;

each R_{12} is independently
hydrogen,
(D)-aryl or
alkyl;

each R_{13} is independently:
hydrogen or
C_1 - C_4 alkyl;

R_{14} is independently selected from the group consisting of:
hydrogen,
halo,
alkyl,
(D)-cycloalkyl,
alkoxy or
phenyl;

R_{15} is independently:
hydrogen,
halo,
alkyl,

(D)-cycloalkyl,
alkoxy or
phenyl;

Cy is selected from aryl, 5- or 6-membered heteroaryl, 5- or 6-membered heterocyclyl or 5- to 7-membered carbocyclyl;

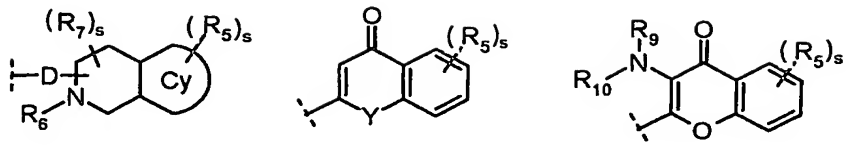
A is a bond or CH_2;
D is a bond or CH_2;
Y is NR_9 or O;
n is 0, 1 or 2;
o is 0 or 1;
p is 0 or 1;
s is 0 – 3
v is 0 or 1.

3. The compound of claim 1 or 2, wherein

each R_1 is independently:
cyano,
nitro,
halo,
alkyl,
(D)-heterocyclyl,
(D)-$N(R_{15})_2$,
(D)-$NR_{15}COR_{15}$,
(D)-$NR_{15}CON(R_{15})_2$,
(D)-$NR_{15}C(O)OR_{15}$ or

(D)-$NR_{15}SO_2R_{15}$;

R_2 is:



R_3 is (CH_2)-phenyl or (CH_2)-naphthyl, substituted with one or two substituents selected from the group consisting of perfluoroalkoxy, halo, alkyl, alkoxy and haloalkyl;

each R_5 is independently:

hydrogen,
halo,
alkyl,
hydroxy,
S-alkyl,
SO_2-alkyl or
alkoxy;

R_6 is hydrogen;

R_7 is hydrogen;

R_9 and R_{10} are each independently:

hydrogen or
alkyl, or
R_9 and R_{10} together with the nitrogen to which they are attached form a 5- to 6-membered ring optionally containing an additional oxygen atom;

R_{12} is hydrogen or (D)-aryl

each R_{13} is independently:
hydrogen,
methyl or
ethyl;

R_{14} is independently:
hydrogen,
halo,
alkyl,
alkoxy or
phenyl;

R_{15} is independently:
hydrogen,
halo,
alkyl,
alkoxy or
phenyl;

Cy is:
aryl or
heteroaryl;

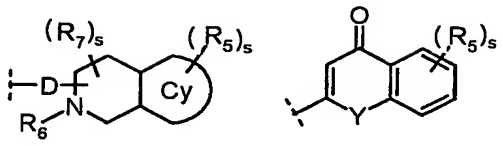
D is a bond;
n is 1 or 2;
o is 0;
p is 0;

s is 0 - 2.

4. The compound of claim 1, 2 or 3 wherein

R_1 is (D)-heterocyclyl;

R_2 is:



R_3 is (CH_2)-phenyl or (CH_2)-naphthyl, unsubstituted or substituted with one or two halogen atoms;

each R_5 is independently:
hydrogen,
isopropyl,
hydroxy,
alkoxy,
S-alkyl or
SO_2-alkyl;

R_6 is hydrogen;

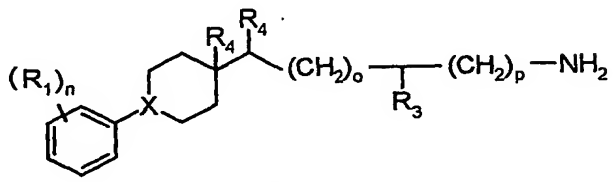
R_7 is hydrogen;

R_9 and R_{10} are each independently:

hydrogen or
alkyl, or
R_9 and R_{10} together with the nitrogen to which they are attached form a 5- to 6-membered ring optionally containing an additional oxygen atom;

Cy is benzene;
s is 0 or 1.

5. An intermediate compound of structural formula (II)



(II)

wherein X, R_1, R_3, R_4, n, o and p are as defined in claim 1.

6. The compound of any of claims 1 to 5 for use as a medicament.

7. Use of the compound of any of claims 1 to 5 for the preparation of a medicament for the treatment or prevention of disorders, diseases or conditions responsive to the inactivation or activation of the melanocortin-4 receptor in a mammal.

8. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of cancer cachexia.

9. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of muscle wasting.

10. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of anorexia.

11. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of anxiety and/or depression.

12. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of obesity.

13. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of diabetes mellitus.

14. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of male or female sexual dysfunction.

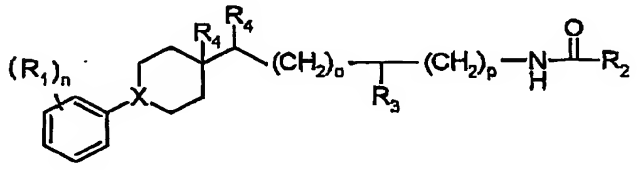
15. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of erectile dysfunction.

16. A pharmaceutical composition which comprises a compound of any of claims 1 to 5 and a pharmaceutically acceptable carrier.

AMENDED CLAIMS
[received by the International Bureau on 12 July 2004 (12.07.04);
original claims 1-16 replaced by amended claims 1-15]

New Claims 1 - 15

1. A compound of structural formula (I):



(I)

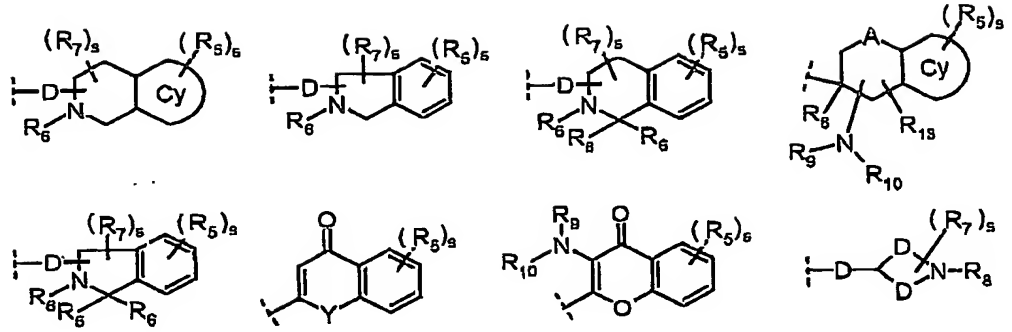
or a pharmaceutically acceptable salt or a solvate thereof, wherein

R_1 is independently:

hydrogen,
hydroxy,
cyano,
nitro,
halo,
alkyl,
alkoxy,
haloalkyl,
(D)-C(O)R_{15},
(D)-C(O)OR_{15},
(D)-C(O)SR_{15},
(D)-C(O)-heteroaryl,

(D)-C(O)-heterocyclyl,
(D)-C(O)N(R_{15})$_2$,
(D)-N(R_{15})$_2$,
(D)-NR_{15}COR_{15},
(D)-NR_{15}CON(R_{15})$_2$,
(D)-NR_{15}C(O)OR_{15},
(D)-NR_{15}C(R_{15})=N(R_{15}),
(D)-NR_{15}C(=NR_{15})N(R_{15})$_2$,
(D)-NR_{15}SO_2R_{15},
(D)-NR_{15}SO_2N(R_{15})$_2$,
(D)-NR_{15}(D)-heterocyclyl,
(D)-NR_{15}(D)-heteroaryl,
(D)-OR_{15},
OSO_2R_{15},
(D)-[O]$_v$(C_3 - C_7 cycloalkyl),
(D)-[O]$_v$(D)aryl,
(D)-[O]$_v$(D)-heteroaryl,
(D)-[O]$_v$(D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen when v=1),
(D)-SR_{15},
(D)-SOR_{15},
(D)-SO_2R_{15} or
(D)-SO_2N(R_{15})$_2$,
wherein alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl and heteroaryl are unsubstituted or substituted;

R_2 is:



R_3 is independently:

(D)-aryl or

(D)-heteroaryl,

wherein aryl and heteroaryl are unsubstituted or substituted;

R_4 is H or a bond;

each R_5 is independently:

hydrogen,

halo,

alkyl,

haloalkyl,

hydroxy,

alkoxy,

S-alkyl,

SO_2-alkyl,

O-alkenyl
S-alkenyl
$NR_{15}C(O)R_{15}$,
$NR_{15}SO_2R_{15}$,
$N(R_{15})_2$,
(D)-cycloalkyl or
(D)-aryl (wherein aryl is phenyl or naphthyl),
(D)-heteroaryl or
(D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen), and
wherein aryl, heteroaryl, heterocyclyl, alkyl or cycloalkyl is unsubstituted or substituted, and two adjacent R_5 may form a 4- to 7-membered ring;

each R_6 is independently:
hydrogen,
alkyl,
C(O)-alkyl,
(D)-aryl or
cycloalkyl;

each R_7 is independently:
hydrogen,
alkyl,
(D)-aryl,
(D)-heteroaryl,
(D)-$N(R_9)_2$,
(D)-$NR_9C(O)$ alkyl,
(D)-NR_9SO_2 alkyl,
(D)-$SO_2N(R_9)_2$,
(D)-$(O)_r$ alkyl,

(D)-(O)$_r$(D)-NR_9COR_8,
(D)-(O)$_r$(D)-$NR_9SO_2R_9$,
(D)-(O)$_r$-heterocyclyl or
(D)-(O)$_r$(alkyl)-heterocyclyl;

each R_8 is independently:
hydrogen,
alkyl,
(D)-aryl,
C(O) alkyl,
C(O)-aryl,
SO_2-alkyl or
SO_2-aryl;

R_9 and R_{10} are each independently:
hydrogen,
alkyl or
cycloalkyl, or
R_9 and R_{10} together with the nitrogen to which they are attached form a 5- to 8-membered ring optionally containing an additional heteroatom selected from O, S and NR_8,
wherein alkyl and cycloalkyl are unsubstituted or substituted;

R_{13} is:
hydrogen or
alkyl;

each R_{15} is independently:
hydrogen,
alkyl,

haloalkyl,
(D)-cycloalkyl,
(D)-aryl (wherein aryl is phenyl or naphthyl),
(D)-heteroaryl or
(D)-heterocyclyl,
wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen, and wherein aryl, heteroaryl, heterocyclyl, alkyl and cycloalkyl is unsubstituted or substituted;

Cy is:
aryl,
5- or 6-membered heteroaryl,
5- or 6-membered heterocyclyl or
5- or 7-membered carbocyclyl;

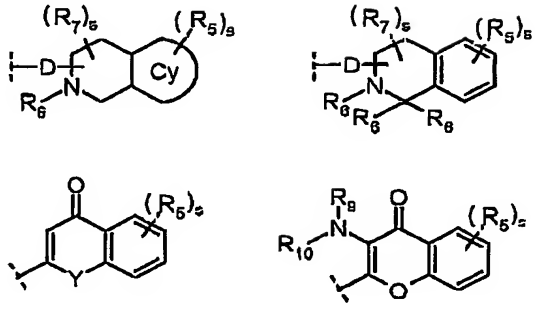
A is a bond, O, $S(O)_u$, NR_8 or CH_2;
D is a bond or alkylene;
X is N or CH;
Y is O or NR_8;
n is 1 - 4;
o is 0 - 2;
p is 0 - 2;
r is 0 or 1;
s is 0 - 5;
u is 0 - 2;
v is 0 or 1.

2. The compound of claim 1, wherein

each R_1 is independently:

hydrogen,
hydroxy,
cyano,
nitro,
halo,
alkyl,
alkoxy,
haloalkyl,
(D)-$N(R_{15})_2$,
(D)-$NR_{15}COR_{15}$,
(D)-$NR_{15}CON(R_{15})_2$,
(D)-$NR_{15}C(O)OR_{15}$,
(D)-$NR_{15}C(R_{15})=N(R_{15})$,
(D)-$NR_{15}C(=NR_{15})N(R_{15})_2$,
(D)-$NR_{15}SO_2R_{15}$,
(D)-$NR_{15}SO_2N(R_{15})_2$ or
(D)-heterocyclyl;

R_2 is:



R_3 is (CH_2)-phenyl or (CH_2)-naphthyl, unsubstituted or substituted with one to three substituents selected from the group consisting of cyano, nitro, perfluoroalkoxy, halo, alkyl, (D)-cycloalkyl, alkoxy and haloalkyl;

each R_5 is independently:
hydrogen,
halo,
alkyl,
haloalkyl,
hydroxy,
alkoxy,
S-alkyl,
SO_2-alkyl,
O-alkenyl or
S-alkenyl;

each R_6 is independently:
hydrogen or
alkyl;

each R_7 is independently:
alkyl,
hydrogen,
(D)-aryl,
(D)-heteroaryl,
(D)-$N(R_9)_2$,
(D)-$NR_9C(O)$alkyl or
(D)-NR_9SO_2alkyl;

R_9 and R_{10} are each independently:

hydrogen,
alkyl or
cycloalkyl, or
R_9 and R_{10} together with the nitrogen to which they are attached form a 5- to 7-membered ring optionally containing an additional heteroatom selected from O, S and NR_6;

each R_{11} is independently:
alkyl,
OR_{12},
(D)-aryl,
(D)-cycloalkyl,
(D)-heteroaryl or
halo;

each R_{12} is independently
hydrogen,
(D)-aryl or
alkyl;

each R_{13} is independently:
hydrogen or
C_1 - C_4 alkyl;

R_{14} is independently selected from the group consisting of:
hydrogen,
halo,
alkyl,
(D)-cycloalkyl,
alkoxy or

phenyl;

R_{15} is independently:
hydrogen,
halo,
alkyl,
(D)-cycloalkyl,
alkoxy or
phenyl;

Cy is selected from aryl, 5- or 6-membered heteroaryl, 5- or 6-membered heterocyclyl or 5- to 7-membered carbocyclyl;

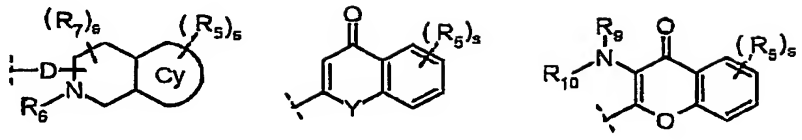
A is a bond or CH_2;
D is a bond or CH_2;
Y is NR_8 or O;
n is 0, 1 or 2;
o is 0 or 1;
p is 0 or 1;
s is 0 – 3
v is 0 or 1.

3. The compound of claim 1 or 2, wherein

each R_1 is independently:
cyano,
nitro,
halo,

alkyl,
(D)-heterocyclyl,
(D)-$N(R_{15})_2$,
(D)-$NR_{15}COR_{15}$,
(D)-$NR_{15}CON(R_{15})_2$,
(D)-$NR_{15}C(O)OR_{15}$ or
(D)-$NR_{15}SO_2R_{15}$;

R_2 is:



R_3 is (CH_2)-phenyl or (CH_2)-naphthyl, substituted with one or two substituents selected from the group consisting of perfluoroalkoxy, halo, alkyl, alkoxy and haloalkyl;

each R_5 is independently:
hydrogen,
halo,
alkyl,
hydroxy,
S-alkyl,
SO_2-alkyl or
alkoxy;

R_6 is hydrogen;

R_7 is hydrogen;

R_9 and R_{10} are each independently:

hydrogen or

alkyl, or

R_9 and R_{10} together with the nitrogen to which they are attached form a 5- to 6-membered ring optionally containing an additional oxygen atom;

R_{12} is hydrogen or (D)-aryl

each R_{13} is independently:

hydrogen,

methyl or

ethyl;

R_{14} is independently:

hydrogen,

halo,

alkyl,

alkoxy or

phenyl;

R_{15} is independently:

hydrogen,

halo,

alkyl,

alkoxy or

phenyl;

Cy is:

aryl or

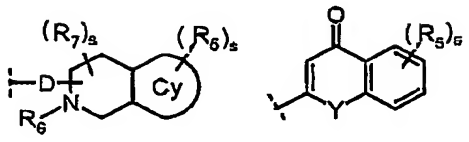
heteroaryl;

D is a bond;
n is 1 or 2;
o is 0;
p is 0;
s is 0 - 2.

4. The compound of claim 1, 2 or 3 wherein

R_1 is (D)-heterocyclyl;

R_2 is:



R_3 is (CH_2)-phenyl or (CH_2)-naphthyl, unsubstituted or substituted with one or two halogen atoms;

each R_5 is independently:
hydrogen,
isopropyl,
hydroxy,
alkoxy,
S-alkyl or
SO_2-alkyl;

R_6 is hydrogen;

R_7 is hydrogen;

R_9 and R_{10} are each independently:
hydrogen or
alkyl, or
R_9 and R_{10} together with the nitrogen to which they are attached form a 5- to 6-membered ring optionally containing an additional oxygen atom;

Cy is benzene;
s is 0 or 1.

5. The compound of any of claims 1 to 4 for use as a medicament.

6. Use of the compound of any of claims 1 to 4 for the preparation of a medicament for the treatment or prevention of disorders, diseases or conditions responsive to the inactivation or activation of the melanocortin-4 receptor in a mammal.

7. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of cancer cachexia.

8. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of muscle wasting.

9. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of anorexia.

10. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of anxiety and/or depression.

11. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of obesity.

12. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of diabetes mellitus.

13. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of male or female sexual dysfunction.

14. Use according to claim 6 for the preparation of a medicament for the treatment or prevention of erectile dysfunction.

15. A pharmaceutical composition which comprises a compound of any of claims 1 to 4 and a pharmaceutically acceptable carrier.